

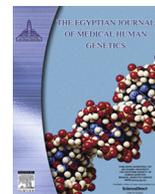
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The Egyptian Journal of Medical Human Genetics

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Cardiomyopathy in Vici syndrome

Dear Editor,

A 7 month old boy was referred to our clinic with provisional diagnosis of Pompe disease because of his Echocardiographic findings of hypertrophic cardiomyopathy. Although the patient had severe hypotonia and increased CPK level characteristics of Pompe disease, other clinical findings made this diagnosis unlikely.

Our patient is the 2nd in order of birth of first cousin parents delivered at full term by vaginal delivery after an uncomplicated pregnancy. The main complaint of the patient was failure to thrive, recurrent chest infections that needed frequent hospital admissions and generalized hypotonia. During his last admission, Echocardiography was done and revealed hypertrophic cardiomyopathy.

On examination, he had failure to thrive, his weight was 3.8 kg (below 3rd percentile), his length was 61 cm (below 3rd percentile) and his skull circumference was 37 cm (below 3rd percentile). The patient had oculocutaneous albinism, sparse scalp hair, micrognathia and high arched palate. Neurologic examination revealed global developmental delay, generalized hypotonia, decreased deep tendon reflexes and preserved superficial reflexes. Sensations were intact. Abdominal examination was clinically normal and he had normal male external genitalia. Family history was unremarkable. Ophthalmology examination revealed foveal hypoplasia, pale optic disc, bilateral ocular albinism and bilateral anterior polar cataract.

Complete blood picture revealed anemia, persistent leucopenia and normal platelets (Hgb: 9.5 g/dL, platelets 415,000/cm³, WBCs 3.600/mm³, lymphocytes: 35%, neutrophils: 49% and monocytes 14%). Total CPK level was 363 U/L (normal 25–130). Liver and Kidney function tests were normal.

Extended metabolic screen, serum lactate, serum ammonia, organic acids in urine, plasma very long chain fatty acids, plasma acid maltase enzyme revealed no abnormalities. EEG revealed focal right frontal – temporal epileptogenic dysfunction. MRI brain revealed agenesis of corpus callosum (ACC), pontine hypoplasia and infracerebellar arachnoid cyst (Fig. 1). Unfortunately, the patient died with severe pneumonia before doing further investigations.

Our patient was diagnosed as Vici syndrome based on the presence of diagnostic clinical criteria including ACC, albinism, cardiomyopathy, immunodeficiency (leucopenia and neutropenia), cataracts, and skeletal myopathy [1]. The syndrome was first described in 1988, in two brothers with ACC, bilateral cataracts,

cleft lip and palate, hypopigmentation of the skin and hair, combined immunodeficiency, and severe psychomotor retardation [2].

Similar to patients with Pompe disease, Vici patients have hypotonia sometimes with elevated muscle enzymes suggesting a muscular origin. This was confirmed by muscle biopsy in nine patients [3]. Vici patients may also have cardiomyopathy which usually develops early in life but sometimes its onset is delayed till childhood. Both hypertrophic and dilated forms were reported [4,5]. Our patient had early onset hypertrophic type of cardiomyopathy.

He also had recurrent respiratory infection which is one of the major symptoms of Vici syndrome which can be explained by cardiomyopathy, hypotonia and variable range of immunodeficiency [6].

One of the differentiating features of Vici syndrome is the CNS anomalies which is absent in Pompe disease. This includes ACC, cerebellar vermal hypoplasia, polymicrogyria/abnormal gyration, cerebral atrophy/hypoplasia, absent septum pellucidum, and hypoplasia of the pons. Our patient had agenesis of corpus callosum, pontine hypoplasia and infra-cerebellar arachnoid cyst [5].

Another differentiating feature is the ocular features which includes cataract, optic nerve hypoplasia, visual impairment and fundus hypopigmentation [3,7]. Our patient had foveal hypoplasia, pale optic disc, bilateral ocular albinism and bilateral anterior polar cataract.

A cardinal feature is the marked oculocutaneous hypopigmentation relative to the familial and ethnic background. Children with Vici syndrome have generally pale skin with light (often very blonde in those of Caucasian origin as detected in our patient) hair, rather than discrete hypopigmented patches [8].

The diagnosis of Vici syndrome is confirmed by finding recessive mutations in the EPG5 gene located at chromosome 18q12.3 and encoding the key autophagy regulator: Ectopic P-Granules protein 5. Autophagy is a fundamental cellular degradative pathway with important roles in the removal of defective proteins and organelles, defense against infections and adaptation to changing metabolic demands [9]. This is done through several steps started by the formation of isolated membranes (phagophores) then fusion with lysosomes (autophagosome) and finally the degradation step (autolysosome) [10]. There is currently no cure for Vici syndrome and management is essentially supportive, aimed at alleviating the effects of extensive multisystem involvement [11].

To conclude, cardiomyopathy is a key sign of Vici syndrome but it should not be confused with Pompe disease because of the neurodevelopmental delay, CNS anomalies and characteristic albinism.

Peer review under responsibility of Ain Shams University.

<https://doi.org/10.1016/j.ejmhg.2017.12.003>

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Fig. 1. MRI brain showing pontine hypoplasia and infracerebellar arachnoid cyst.

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Available online 12 January 2018

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